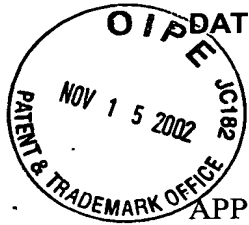


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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANTS: Mary E. Gerritsen, et al. DOCKET NO.: 09800080-0035  
SERIAL NO.: 09/865,859 GROUP ART UNIT: 1625  
DATE FILED: May 25, 2001 EXAMINER: Not Yet Known  
INVENTION: "METHOD OF INHIBITING ANGIOGENESIS"

4  
Yes  
11-26

**INFORMATION DISCLOSURE STATEMENT**

Commissioner of Patents  
Washington, DC 20231

Dear Sir:

In accordance with the provisions of 37 C.F.R. § 1.56, Applicants request that citation and examination of the references identified on the attached PTO-1449 form, copies of which are not enclosed herewith, in accordance with 37 C.F.R. §1.98, be made during the course of examination of the above-referenced application for United States Letters Patent. Copies have not been provided since all the references cited were previously cited in the parent application to which this application claims priority, Application Serial No. 09/443,010. Please charge the \$180 filing fee to American Express Account No. 3785-716974-01002. A Credit Card Payment Form is attached. A duplicate copy of this paper is attached.

Respectfully submitted,

Paul E. Rauch, Ph.D.  
Registration No. 38,591  
Attorney for Applicant

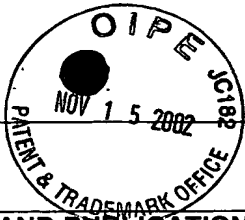
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P. O. BOX 061080  
WACKER DRIVE STATION, SEARS TOWER  
CHICAGO, IL 60606  
(312) 876-7440 (Phone)  
(312) 876-7934 (Fax)  
prauch@sonnenschein.com (Email)

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FORM PTO-1449	SERIAL NO.: 09/865,859	DOCKET NO. 09800080-0035
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(use several sheets if necessary)		APPLICANT: Mary E. Gerritsen, et al.

REFERENCE DESIGNATION		U.S. PATENT DOCUMENTS				
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS/ SUBCLASS	FILING DATE
	A1	4,287,200	01-09-81	Kawamatsu, et al.		
	A2	4,340,605	20-07-82	Kawamatsu, et al.		
	A3	4,438,141	20-03-84	Kawamatsu, et al.		
	A4	4,444,779	24-04-84	Kawamatsu, et al.		
	A5	4,461,902	24-07-84	Kawamatsu, et al.		
	A6	4,572,912	25-02-86	Yoshioka, et al.		
	A7	4,687,777	18-08-87	Meguro, et al.		
892- 11	✓ A8	4,703,052	27-10-87	Eggler, et al.		
	✓ A9	4,725,610	16-02-88	Meguro, et al.		
	A10	4,810,804	07-03-89	Chandraratna, R.		
	A11	4,873,255	10-10-89	Yoshioka, et al.		
	A12	4,897,393	30-01-90	Iijima, et al.		
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897	✓ A14	4,918,091	17-04-90	Cantello, et al.		
	A15	4,948,900	14-08-90	Iijima, et al.		
	A16	5,002,953	26-03-91	Hindley, R.		
	A17	5,061,717	29-10-91	Clark, et al.		
	A18 ✓	5,120,754	09-06-92	Clark, et al.		
	A19	5,132,317	21-07-92	Cantello, et al.		
	A20	5,194,443	16-03-93	Hindley, R.		
	A21	5,223,522	29-06-93	Clark, et al.		
	A22	5,232,925	03-08-93	Hindley, R.		
	A23	5,260,445	09-11-93	Hindley, R.		
	A24	5,399,586	21-03-95	Davies, et al.		
	A25	5,457,109	10-10-95	Antonucci, et al.		23-08-94
	A26	5,466,861	14-11-95	Dawson, et al.		
	A27 ✓	5,478,852	26-12-95	Olefsky, et al.		23-08-94
	A28	5,599,826	04-02-97	Mertens, et al.		19-05-94
	A29	5,646,169	08-07-97	Hindley, et al.		01-06-95
	A30	5,686,596	11-11-97	Mukherjee		
	A31	5,700,682	23-12-97	Mak, et al.		
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	A33	5,710,004	20-01-98	Evans, et al.		

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REFERENCE DESIGNATION		U.S. PATENT DOCUMENTS				
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	A34	5,714,595	03-02-98	Mak, et al.		
	A35	5,770,378	23-06-98	Hwang, et al.		
	A36	5,770,382	23-06-98	Hwang, et al.		
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	A38	5,780,676	14-07-98	Boehm, et al.		
	A39	5,811,439	22-09-98	Ogawa, et al.		18-12-96
	A40	5,814,647	29-09-98	Urban, et al.		04-03-97
	A41	5,824,685	20-10-98	Campochiaro, et al.		
	A42	5,902,726	11-05-99	Kliwer, et al.		
	A43	5,925,657	20-07-99	Seed, et al.		
	A44	6,034,110	07-03-00	Nagpal, et al.		

FOREIGN PATENT DOCUMENTS						
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS/ SUBCLASS	TRANSLATION YES NO
	B1	EPO 953,355	03-11-99	Europe		
	B2	JP 4-69383	04-03-92	Japan		
	B3	JP 62-234085	14-10-87	Japan		
	B4	WO 00/00194	06-01-00	WIPO		
	B5	WO 89/08651	21-09-89	WIPO		
	B6	WO 91/07107	30-05-91	WIPO		
	B7	WO 92/02520	20-02-92	WIPO		
	B8	WO 94/01433	20-01-94	WIPO		
	B9	WO 95/35108	28-12-95	WIPO		
	B10	WO 97/10819	27-03-97	WIPO		
	B11	WO 97/45141	04-12-97	WIPO		
	B12	WO 97/46238	11-12-97	WIPO		
	B13	WO 98/25598	18-06-98	WIPO	31/00	X
	B14	WO 98/29113	09-07-98	WIPO		
	B15	WO 98/39006	11-09-98	WIPO	31/495	X
	B16	WO 98/57631	23-12-98	WIPO		
	B17	WO 99/34783	15-07-99	WIPO		
	B18	WO 99/48529	30-09-99	WIPO		

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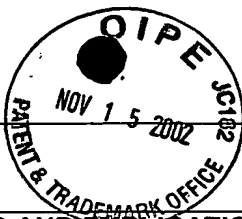
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EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
C1	Bishop-Bailey et al., "Endothelial Cell Apoptosis Induced by the Peroxisome Proliferator-activated Receptor (PPAR) Ligand 15-Deoxy- $\Delta^{12,14}$ -prostaglandin $\Delta^2$ " Journal of Biological Chemistry 274(24):17042-17048(06 11, 1999)
C2	Brown et al., "Association between expression of activated 72-kilodalton gelatinase and tumor spread in non-small-cell lung carcinoma" Journal of the National Cancer Institute 85(7): 574-578 (Apr 7, 1993)
C3	Danehower et al., "Troglitazone inhibits proliferation of microvascular endothelial cells; implications for diabetic retinopathy" Diabetologia (Abstract No. 1581 presented at the 16 <sup>th</sup> International Diabetes Federation Congress held in Helsinki, Finland on July 20-25, 1997) 40(suppl. 1):A402 (1997)
C4	Davis and Camarillo, "An $\Delta^{12/14}$ Integrin-dependent pinocytic mechanism involving intracellular vacuole formation and coalescence regulates capillary lumen and tube formation in three-dimensional collagen matrix" Experimental Cell Research 224(1):39-51 (Apr 10, 1996)
C5	Elstner et al., "Ligands for peroxisome proliferator-activated receptor $\Delta^{147}$ and retinoic acid receptor inhibit growth and induce apoptosis of human breast cancer cells in vitro and in BNX mice" Proc. Natl. Acad. Sc. USA 95(15):8806-8811 (Jul 21, 1998)
C6	Ferrara and David-Smyth, "The biology of vascular endothelial growth factor" Endocrine Reviews 18(1):4-25 (1997)
C7	Fisher et al., "Interstitial collagenase is required for angiogenesis in vitro" Developmental Biology 162(2):499-510 (Apr 1994)
C8	Fong et al., "Role of the Fit-1 receptor tyrosine kinase in regulating the assembly of vascular endothelium" Nature 376:66-70 (1995)
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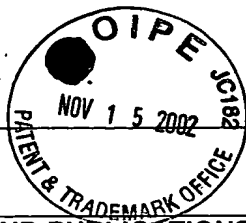
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EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
C10	Forman et al., "Hypolipidemic drugs, polyunsaturated fatty acids, and eicosanoids are ligands for peroxisome proliferator-activated receptors \141 and \144" Proc. Natl. Acad. Sci. USA 94(9):4312-4317 (Apr 29, 1997)
C11	Gralinski et al., "Effects of Troglitazone and Pioglitazone on Cytokine-Mediated Endothelial Cell Proliferation in Vitro" Journal of Cardiovascular Pharmacology, Philadelphia:Lippincott-Raven Publishers Vol. 31:909-913 (1998)
C12	Haas et al., "Three-dimensional type I collagen lattices induce coordinate expression of matrix metalloproteinases MT1-MMP and MMP-2 in microvascular endothelial cells" Journal of Biological Chemistry 273(6):3604-3610 (Feb 6, 1998)
C13	Hanemaaljer et al., "Regulation of matrix metalloproteinase expression in human vein and microvascular endothelial cells. Effects of tumour necrosis factor\141, interleukin 1 and phorbol ester" Biochemical Journal 296(Pt 3):803-809 (Dec 15, 1993)
C14	Healy et al., "Angiogenesis: a new theory for endometriosis" Human Reproduction Update 4(5):736-740 (Sep-Oct 1998)
C15	Hiraoka et al., "Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins" Cell 95(3):365-377 (Oct 30, 1998)
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C18	Issemann and Green, "Activation of a member of the steroid hormone receptor superfamily by peroxisome proliferators" Nature 347(6294):645-650 (Oct 18, 1990)

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EXAMINER INITIAL	OTHER ART (Including Author, Title, Date, Pertinent Pages, etc.)
C19	Itoh et al., "Unaltered secretion of $\beta$ 142-amyloid precursor protein in gelatinase A (matrix metalloproteinase 2)-deficient mice" Journal of Biological Chemistry 272(36):22389-22392 (Sep 5, 1997)
C20	Jiang et al., "PPAR- $\gamma$ agonists inhibit production of monocyte inflammatory cytokines" Nature 391(6662):82-86 (Jan 1, 1998)
C21	Johnsen et al., "Cancer invasion and tissue remodeling: common themes in proteolytic matrix degradation" Current Opinion in Cell Biology 10(5):667-671 (Oct 1998)
C22	Kliwer, S.A., "A prostaglandin $\text{IP}_{2}$ nor metabolite binds peroxisome proliferator-activated receptor $\gamma$ 147 and promotes adipocyte differentiation" Cell 83:813-819 (1995)
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C24	Lamoreaux et al., "Vascular endothelial growth factor increases release of gelatinase A and decreases release of tissue inhibitor of metalloproteinases by microvascular endothelial cells in vitro" Microvascular Research 55(1):29-42 (Jan 1998)
C25	Mackay et al., "Effect of phorbol ester and cytokines on matrix metalloproteinase and tissue inhibitor of metalloproteinase expression in tumor and normal cell lines" Invasion & Metastasis 12(3-4):168-184 (1992)
C26	Marx et al., "Macrophages in human atheroma contain PPAR $\gamma$ 147: Differentiation-dependent peroxisomal proliferator-activated receptor $\gamma$ 147 (PPAR $\gamma$ 147) expression and reduction of MMP-9 activity through PPAR $\gamma$ 147 activation in mononuclear phagocytes in vitro" American Journal of Pathology 153(1):17-23 (Jul 1998)
C27	Marx et al., "Peroxisome proliferator-activated receptor gamma activators inhibit gene expression and migration in human vascular smooth muscle cells" Circulation Research 83(11):1097-1103 (Nov 30, 1998)

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C28	Moses, M., "The regulation of neovascularization of matrix metalloproteinases and their inhibitors" Stem Cells 15(3):180-189 (1997)
C29	Motojima, K., "Toward the treatment of obesity. Role of PPAR gamma in adipogenesis" Tanpakushitasu Kakusan Koso (Abstract only) 40(13):1936-1941 (1995)
C30	Mukherjee et al., "Identification, characterization, and tissue distribution of human peroxisome proliferator-activated receptor (PPAR) isoforms PPAR\1472 versus PPAR\1471 and activation with retinoid X receptor agonists and antagonists" Journal of Biological Chemistry 272(12):8071-8076 (Mar 21, 1997)
C31	Mukherjee et al., "Sensitization of diabetic and obese mice to insulin by retinoid X receptor agonists" Nature 386(6623):407-410 (Mar 27, 1997)
C32	Murphy et al., "Tissue inhibitor of metalloproteinases-2 inhibits bFGF-induced human microvascular endothelial cell proliferation" Journal of Cellular Physiology 157(2):351-358 (Nov 1993)
C33	Palmer and Wolf, "cis-parinaric acid is a ligand for the human peroxisome proliferator activated receptor\147: development of a novel spectrophotometric assay for the discovery of PPAR\147 ligands" FEBS Letters 431(3):476-480 (Jul 24, 1998)
C34	Pershad Singh et al., "Ophthalmic uses of PPAR-gamma . . ." Caplus 132:73666 (01 6, 2000)
C35	Puyraimond et al., "Examining the relationship between the gelatinolytic balance and the invasive capacity of endothelial cells" Journal of Cell Science 112(Pt 9):1283-1290 (May 1999)
C36	Qian et al., "Thrombospondin-1 modulates angiogenesis in vitro by up-regulation of matrix metalloproteinase-9 in endothelial cells" Experimental Cell Research 235(2):403-412 (Sep 15, 1997)
C37	Ricote et al., "The peroxisome proliferator-activated receptor-\147 is a negative regulator of macrophage activation" Nature 391(6662):79-82 (Jan 1, 1998)

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C38	Sarraf et al., "Differentiation and reversal of malignant changes in colon cancer through PPAR\147" Nature Medicine 4(9):1046-1052 (Sep 1998)
C39	Schnaper et al., "Type IV collagenase(s) and TIMPs modulate endothelial cell morphogenesis in vitro" Journal of Cellular Physiology 156(2):235-246 (Aug 1993)
C40	Spiegelman, B., "PPAR-\147: adipogenic regulator and thiazolidinedione receptor" Diabetes 47(4):507-514 (Apr 1998)
C41	Staels et al., "Activation of human aortic smooth-muscle cells is inhibited by PPAR\141 but not by PPAR\147 activators" Nature 393(6687):790-793 (Jun 25, 1998)
C42	Stetler-Stevenson, W., "Matrix metalloproteinases in angiogenesis; a moving target for therapeutic intervention" Journal of Clinical Investigation 103(9):1237-1241 (May 1999)
C43	Vu et al., "MMP-9/gelatinase B is a key regulator of growth plate angiogenesis and apoptosis of hypertrophic chondrocytes" Cell 93(3):411-422 (May 1, 1998)
C44	Westermarck and Kahari, "Regulation of matrix and metalloproteinase expression in tumor invasion" FASEB Journal 13(8):781-792 (May 1999)
C45	Xin et al., "Peroxisome proliferator-activated receptor gamma (PPAR\147) ligands are potent inhibitors of angiogenesis" FASEB Journal (Abstract #27.4 presented at the Annual Meeting of the Professional Research Scientists for Experimental Biology held in Wash. D.C. on Apr. 17-21, 1999.) 13(4 Part 1):A39 (1999)
C46	Xin et al., "Peroxisome proliferator-activated receptor\147 ligands are potent inhibitors of angiogenesis in vitro and in vivo" Journal of Biological Chemistry 274(13):9116-9121 (Mar 26, 1999)
C47	Yamada et al., "Angiogenic effect of lipid hydroperoxide on bovine aortic endothelial cells" J. Clin. Biochem. Nutr. 25(3):121-130 (1998)

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